

Figure 1

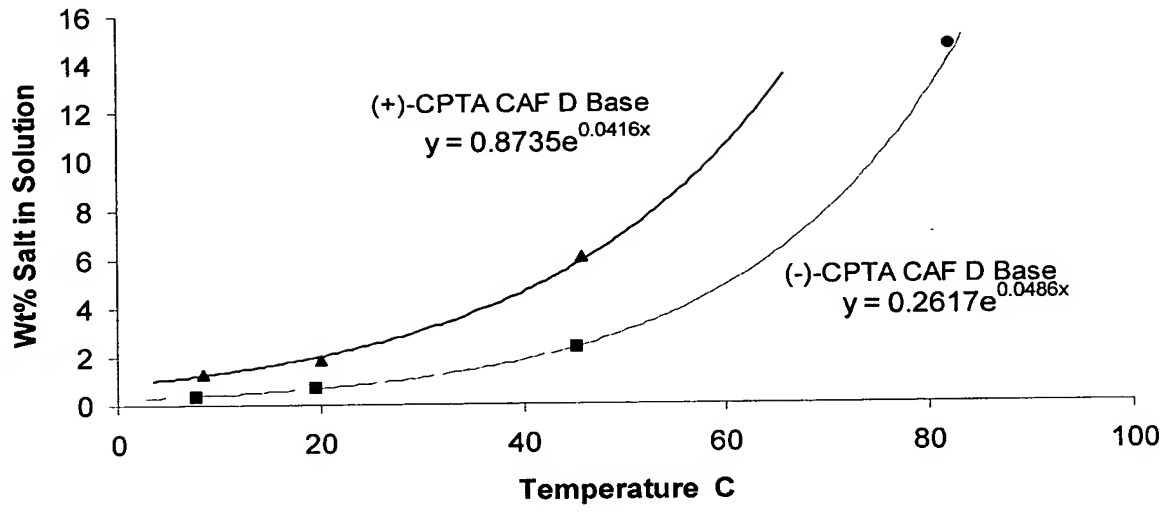


Figure 2

Exp. #	Charge		Nucl'n Temp.	Isolation Temp & Hold Time	Product Isolation: Ratio of % (-)-CPTA		Calculated %Yield of (-)-CPTA	Comments
	g iPA/ gCPTA	mole base/ mole CPTA			Crystal	M.L.		
1	4.11	0.57	61°	17° + 6hr	79.9	27.0	69.5	(+)-Salt nucleation at 22°
2	4.11	0.55	59°	22° + 8hr	77.9	28.3	68.2	(+)-Salt nucleation after 1 hr at 22°
3	4.11	0.90	59°	40°	99.2	27.7	61.9	initially added 0.15 eq. triethylamine
4	5.50	0.75	61°	22° + 10hr	66.4	30.7	71.8	(+)-Salt nucleation at 40°
				to 28°	68.2	28.8	73.4	
				to 35°	71.4	29.1	70.6	
				to 43°	77.0	29.9	65.7	
				to 51°	95.0	30.3	57.9	
				to 55°	99.4	33.0	50.9	
5	4.11	0.52	61°	13° + 8hr	99.7	20.9	73.6	(+)-Salt nucleation 3 hr after sample
				+ 30hr (13°)	83.3	24.9	71.6	
6	3.14	0.52	59°	1°	98.7	23.5	69.6	
				+20hr(1°)	98.2	19.4	76.3	
				to 17° + 9hr	81.2	25.3	71.8	
7	5.50	0.90	64°	3° + 1hr	66.4	25.5	79.6	initially added 0.04 eq. KOH
				to 22° + 10hr	~56	25.5	90.0	
8	3.53	0.55	59°	22° + 5hr	78.6	26.0	71.7	(+)-Salt nucleation at 30°
9	3.93	0.45	59°	22° + 4hr	99.6	24.3	68.0	
				+ 12hr (22°)	99.5	22.9	70.4	
				(22°) + 3hr	89.4	24.6	70.1	(+)-Salt nucleating, not at equilibrium
		0.52 (added base)		(22°) + 22hr	84.3	25.9	69.6	
		0.49 (added CPTA)						
10	3.53	0.52	59°	22° + 10hr	73.9	25.5	74.8	(+)-Salt nucleation at 25°
11	3.93	0.45	54°	22° + 14hr	99.1	22.6	71.0	
		0.48 (added base)		22° + 24hr	89.2	24.7	70.0	
12	3.93	0.43	52°	21°	99.5	27.5	62.2	
				+ 16hr (21 °)	99.4	23.9	68.7	seeded with (+)-Salt after sample
				+8hr(22°)	99.3	23.7	69.1	
				22° + 14hr	98.9	22.5	71.2	seeded with (+)-Salt after sample
		0.45 (added base)		+6hr(22°)	98.7	22.3	71.61	
		0.47 (added base)		22° + 14hr	96.8	21.9	72.6	seeded with (+)-Salt after sample
13	3.14	0.38	59°	+ 23hr (22°)	92.3	23.4	71.3	
				17° + 8hr	99.4	27.2	62.8	
				to -10° + 19hr	99.8	24.3	67.9	seeded with (+)-Salt after reaching 10°

Figure 3

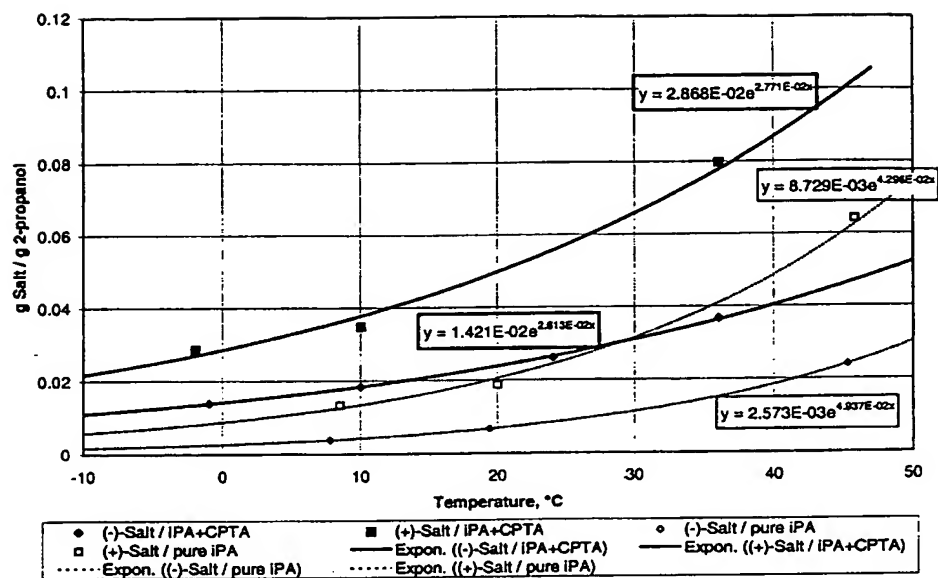


Figure 4

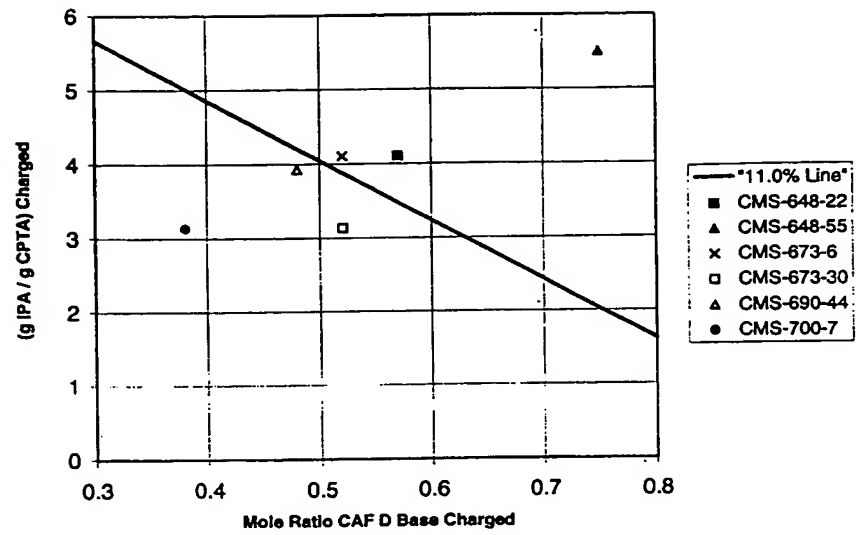


Figure 5

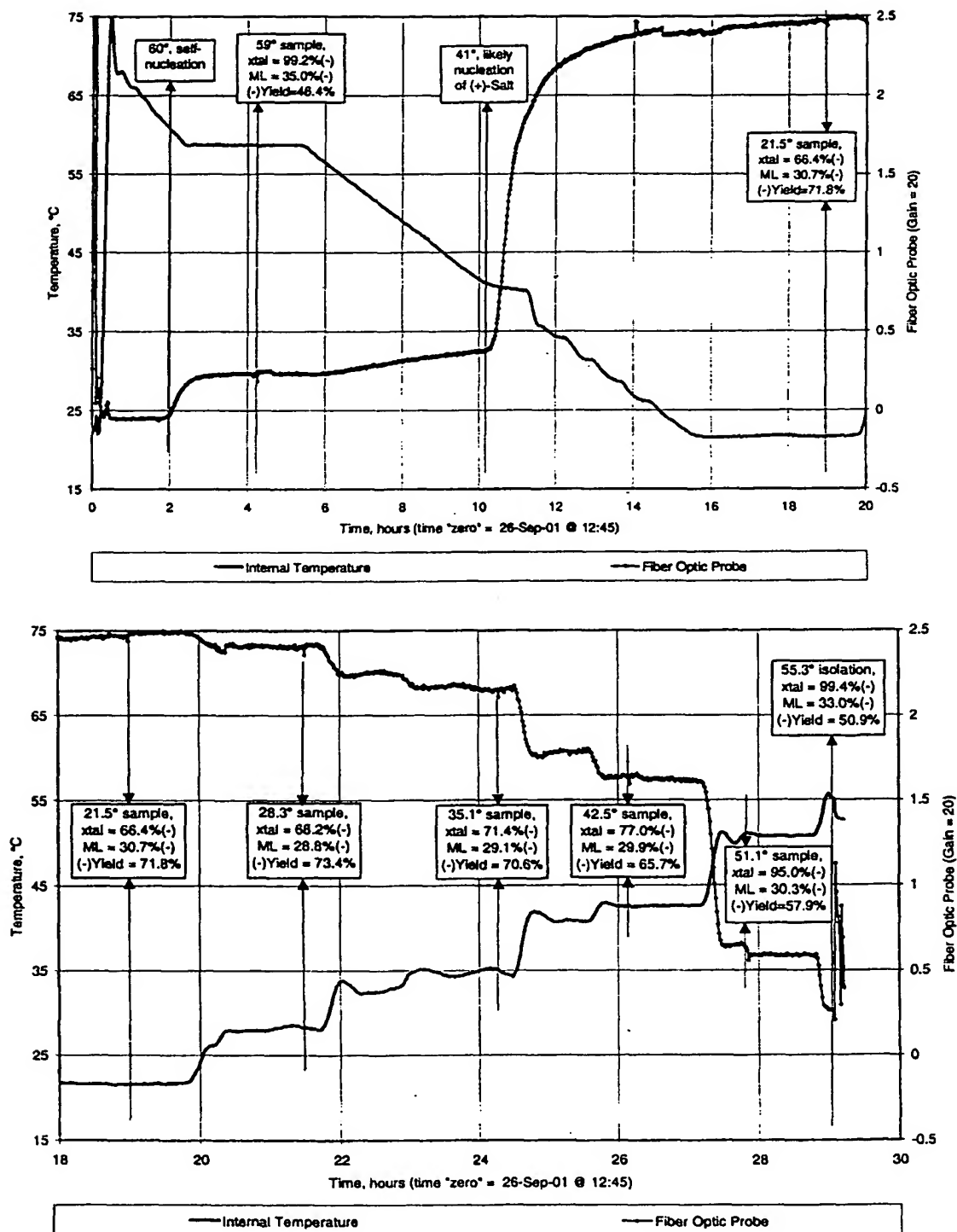


Figure 6

<u>Temperature</u>	<u>Measured Component</u>	<u>Experimental Result</u>	<u>Calculation By Model</u>
21.5 °C	Ratio % (-)-CPTA in crystal	66.4%	63.9%
	Ratio % (-)-CPTA in mother liquor	30.7%	28.5%
	% (-)-CPTA yield	71.8%	72.8%
28.3 °C	Ratio % (-)-CPTA in crystal	68.2%	68.2%
	Ratio % (-)-CPTA in mother liquor	28.8%	28.7%
	% (-)-CPTA yield	73.4%	73.6%
35.1 °C	Ratio % (-)-CPTA in crystal	71.4%	71.4%
	Ratio % (-)-CPTA in mother liquor	29.1%	28.9%
	% (-)-CPTA yield	70.6%	70.8%
42.5 °C	Ratio % (-)-CPTA in crystal	77.0%	76.7%
	Ratio % (-)-CPTA in mother liquor	29.9%	29.1%
	% (-)-CPTA yield	65.7%	67.4%
51.1 °C	Ratio % (-)-CPTA in crystal	95.0%	87.3%
	Ratio % (-)-CPTA in mother liquor	30.3%	29.2%
	% (-)-CPTA yield	57.9%	62.4%
55.3 °C	Ratio % (-)-CPTA in crystal	99.4%	96.1%
	Ratio % (-)-CPTA in mother liquor	33.0%	29.3%
	% (-)-CPTA yield	50.9%	59.6%

Figure 7

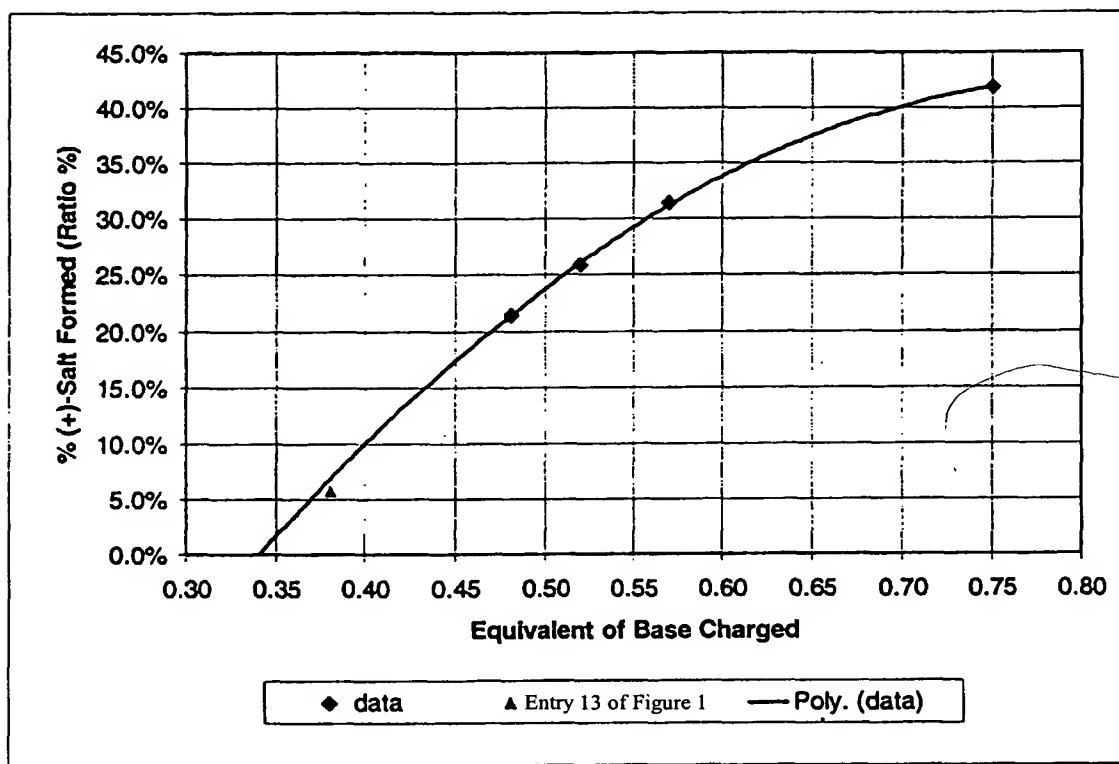


Figure 8

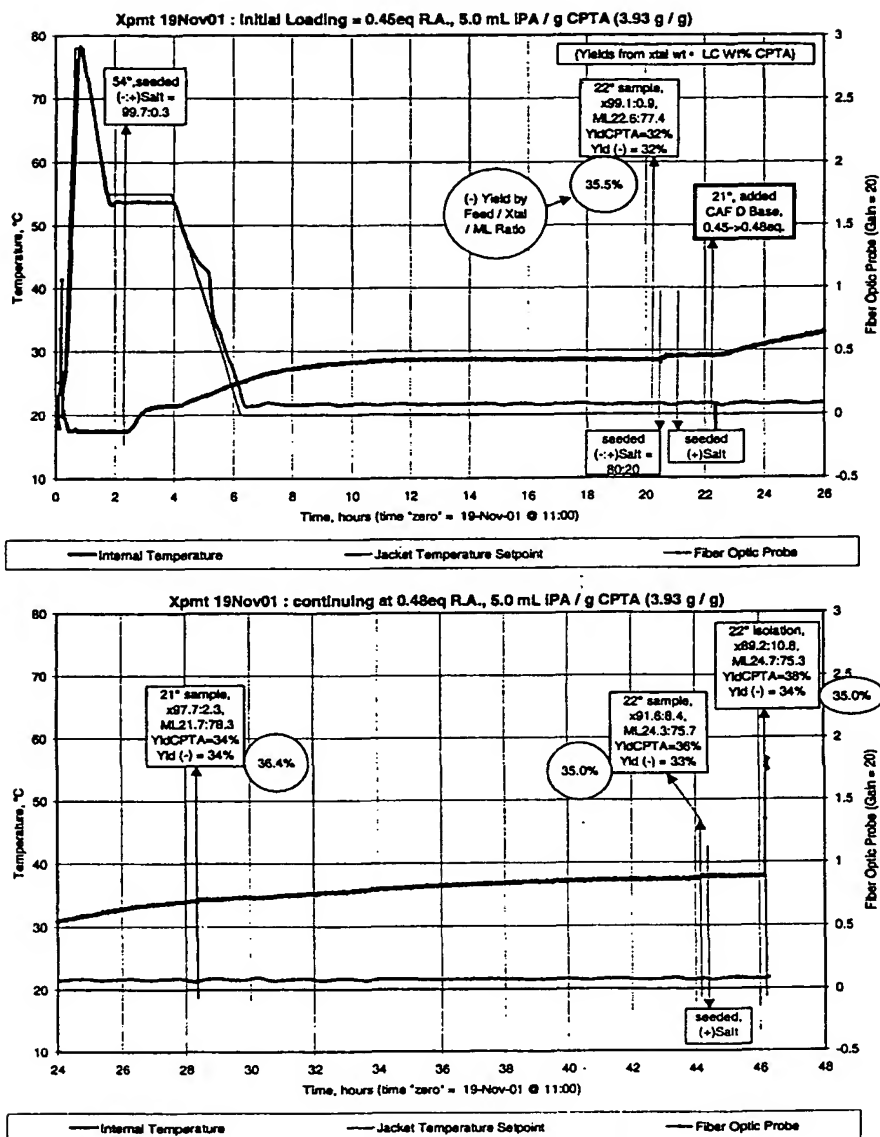


Figure 9

<u>Component</u>	<u>Normalized Wt% (as CPTA) in Mother Liquor</u>	
	<u>By Work-up</u>	<u>By Model</u>
(-)-Salt	28%	20%
(+)-Salt	41%	44%
(-)-CPTA	7%	9%
(+)-CPTA	24%	27%

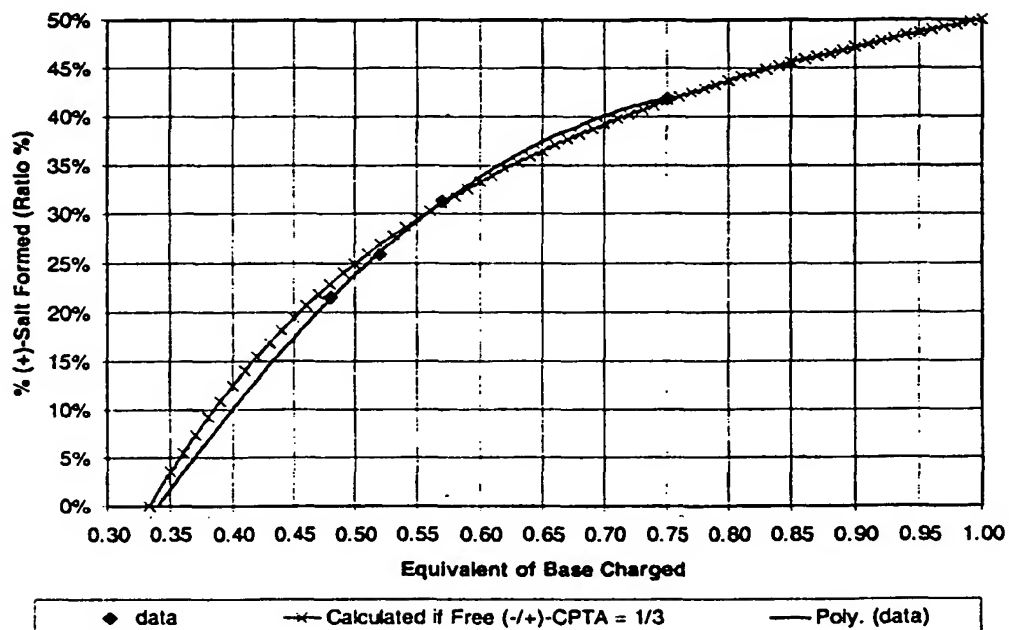


Figure 10A

(-)-CPTA • CAF D Base Salt : m.p. 180½-181½												
Calculated Values												
Solvent	Temp. °C	grams tare	grams w/soln	grams evap'd	grams soln	grams volat. solv	grams solids	grams CPTA	grams solute	Wt% solute	wt% solute in evapSoln	g solute/ g evap solv
iPA w/CPTA	36	17.2900	18.0100	17.3895	0.7200	0.6205	0.0995	0.0767	0.0228	3.17%	3.55%	0.036755
iPA w/CPTA	24	16.7808	17.5728	16.8840	0.7920	0.6888	0.1032	0.0851	0.0181	2.28%	2.56%	0.026226
iPA w/CPTA	10	17.2556	18.1769	17.3702	0.9213	0.8067	0.1146	0.0997	0.0149	1.62%	1.81%	0.01846
iPA w/CPTA	-1	17.1063	17.9898	17.2131	0.8835	0.7767	0.1068	0.0960	0.0108	1.22%	1.37%	0.013905
EtOH w/CPTA	36	17.1900	17.9419	17.3577	0.7519	0.5842	0.1677	0.0912	0.0765	10.18%	11.58%	0.130959
EtOH w/CPTA	24	17.2524	17.9330	17.3913	0.6806	0.5517	0.1289	0.0861	0.0429	6.29%	7.20%	0.077541
EtOH w/CPTA	10	17.2977	18.1608	17.4587	0.8631	0.7021	0.1610	0.1096	0.0514	5.96%	6.82%	0.073212
EtOH w/CPTA	-1	17.1536	18.2098	17.3383	1.0562	0.8715	0.1847	0.1360	0.0487	4.61%	5.29%	0.055833

(+)CPTA • CAF D Base Salt												
Calculated Values												
Solvent	Temp. °C	grams tare	grams w/soln	grams evap'd	grams soln	grams solvent	grams solids	grams CPTA	grams solute	Wt% solute	wt% solute in evapSoln	g solute/ g evap solv
iPA w/CPTA	-2	17.2325	17.8545	17.3147	0.6220	0.5398	0.0822	0.0667	0.0155	2.49%	2.79%	0.028679
iPA w/CPTA	10	17.1810	17.7942	17.2649	0.8132	0.5293	0.0839	0.0654	0.0185	3.01%	3.37%	0.034911
iPA w/CPTA	22	17.2838	18.0462	17.4053	0.7624	0.6409	0.1215	0.0792	0.0423	5.55%	6.19%	0.065977
iPA w/CPTA	36	17.1474	17.8978	17.2742	0.7502	0.6234	0.1268	0.0771	0.0497	6.63%	7.39%	0.079801
iPA w/CPTA	10	17.2816	17.4692	17.3074	0.1876	0.1618	0.0258	0.0200	0.0058	3.09%	3.46%	0.035856
EtOH w/CPTA	-2	17.3289	18.5380	17.6105	1.2091	0.9275	0.2816	0.1448	0.1368	11.32%	12.85%	0.147512
EtOH w/CPTA	10	17.2118	17.9940	17.4089	0.7822	0.5851	0.1971	0.0913	0.1058	13.52%	15.31%	0.180765
EtOH w/CPTA	22	17.2095	18.0054	17.4362	0.7959	0.5692	0.2267	0.0889	0.1378	17.32%	19.50%	0.242178
EtOH w/CPTA	36	17.2133	17.9657	17.4487	0.7524	0.5170	0.2354	0.0807	0.1547	20.56%	23.03%	0.299219

Experimental Data for Figure 6

Eq. Base	Predicted <i>k</i>	Regression <i>k</i> used	Regression % (+)-Salt	Free CPTA, Ratio % (+)
0.75	<1	0.68	41.9	25.8
0.57	<1	0.85	31.4	25.3
0.52	<1	0.70	25.7	23.7
0.52	>1	0.60	26.1	24.1
0.48	>1	0.50	21.5	23.7

Figure 10B

[illegible]

Figure 11

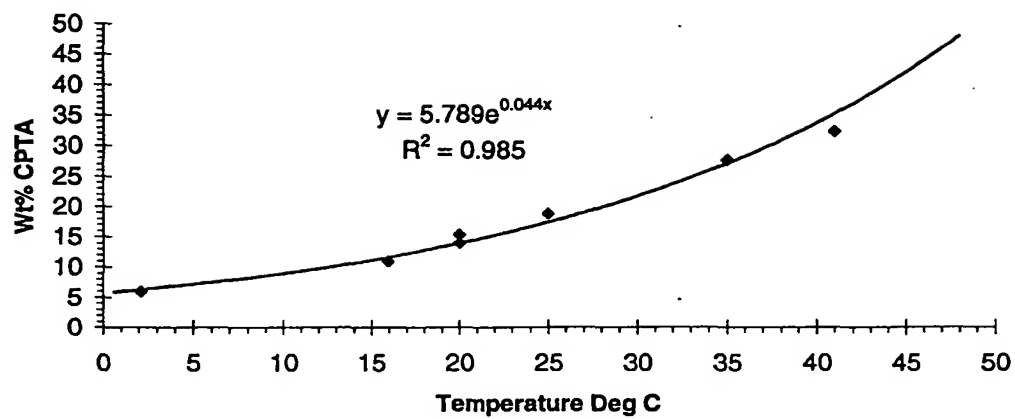


Figure 12

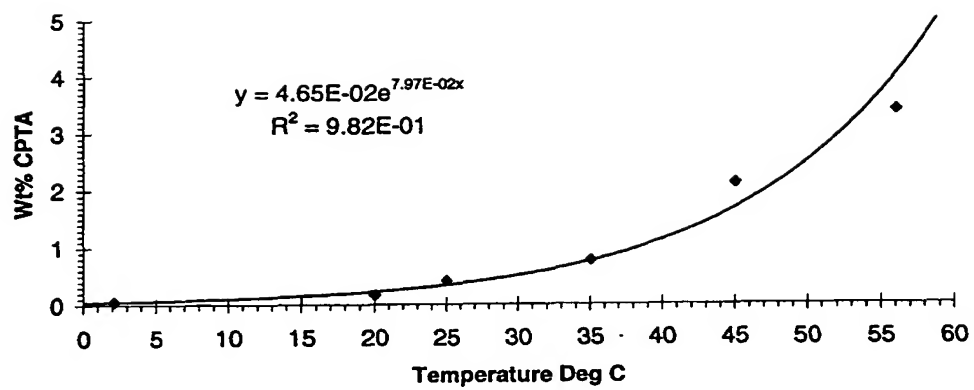


Figure 13

Exp. #	MolRatio Base	g IPA/ g CPTA	Cool at °C/min	Final T °C	Solid % (-)	Solid % (+)	M.L. % (-)	M.L. % (+)	%Yield Calc	%Yield Overall	%Yield Actual
1	0.53	4.00	0.25	4	90.72	9.28	20.61	79.39	41.9		
Recrystallization		4.00	0.25-1.0	2	99.38	0.62	42.60	57.40	84.7	35.5	34.5
2	0.50	6.17	0.05	-3	98.05	1.95	24.05	75.95	35.1	35.1	33.6
3	0.53	4.00	0.25	0	73.14	26.86	28.88	71.12	47.7		
Recrystallization		4.00	1.0	11	98.20	1.80	22.62	77.38	66.8	31.9	33.0
4	0.54	4.00	0.25	-4	79.72	20.28	26.62	73.38	44.0		
Recrystallization		3.63	0.08	4	99.07	0.93	23.22	76.78	74.5	32.8	32.8
5	0.53	4.00	0.5	-11	93.70	6.30	26.00	74.00	35.4		
Recrystallization		3.93	0.5	-3	99.68	0.33	46.42	53.58	88.8	31.5	31.6
6	0.53	3.98	0.25	-3	90.88	9.12	26.95	73.05	36.1		
Recrystallization		4.98	0.1	4	99.42	0.58	23.85	76.15	88.7	32.0	31.5
7	0.54	4.08	0.3	-3	96.00	4.00	nd	nd	-		
Recrystallization		4.24	0.4	4	99.86	0.14	57.41	42.59	90.9	-	31.2
8	0.53	4.00	0.25	-8	73.54	26.46	28.09	71.91	48.2		
Recrystallization		3.96	0.3	11	98.57	1.43	21.84	78.16	67.4	32.5	31.1
9	0.50	3.88	0.08	-7	76.83	23.17	28.96	71.04	43.9		
Recrystallization		4.62	0.5	5	98.48	1.52	24.91	75.09	70.6	31.0	30.7
10	0.50	3.90	0.05	0	96.15	3.85	26.07	73.93	34.1		
Recrystallization		4.80	0.3	3	99.86	0.14	70.32	29.68	87.4	29.9	30.6
11	0.55	6.16	0.2	5	73.92	26.08	nd	nd	-		
Recrystallization		4.38	0.08	12	99.31	0.69	41.08	58.92	56.4	-	29.1
12	0.56	4.99	0.1	2	78.92	21.08	28.04	71.96	43.2		
Recrystallization		5.00	0.25	4	84.47	15.53	29.29	70.71	89.9	(38.8)	(38.3)
Recrystallization		5.00	0.25	12	99.44	0.56	30.30	69.70	78.4	30.4	28.2

nd – Not Determined

Figure 14

Exp. # (Fig. 1)	Initial T °C	Rate °C/min	Final T °C	Hrs at < 10 °C	Holding Period Profile	Solid		M.L.		% Yield (-)-CPTA
						% (-)	% (+)	% (-)	% (+)	
1	60	0.25	4	14	13h at 4C	90.72	9.28	20.61	79.39	38.0
8	60	0.25	-5	20	11 h to 10C; 3h to -8C, 5h at -8C	73.54	26.46	28.09	71.91	35.5
4	55	0.25	-4	3	1h at -4C	79.72	20.28	26.62	73.38	35.1
3	60	0.25	-2	16	11h to 10C; 1h to -2C, 4h at -2C	73.14	26.86	28.88	71.12	34.9
2	55	0.05	-3	5	1h at -3C	98.05	1.95	24.05	75.95	34.4
12	55	0.10	1	13	9h to 10C; 1h to 1C; 4h at 1C	78.92	21.08	28.04	71.97	34.1
9	65	0.075	0	8	3h at 0C; 1h to -7C; 2h at -7C	76.83	23.17	28.96	71.04	33.8
5	60	0.5	-11	2.5	1.5h at -11C	93.70	6.30	26.00	74.00	33.2
10	55	0.05	0	4	1h at 0C	96.15	3.85	26.07	73.93	32.8
6	55	0.25	-3	2	1h at -3C	90.88	9.12	26.95	73.05	32.8

Figure 15

	%ee		HPLC Area% Crude		HPLC Area% Isolated		Yield	mol % in ML	
	CPTA	(-)-halofenate	CPTA	Halofenate	CPTA	Halofenate		CPTA	Halofenate
1	97.1	99.9	6.1	85.2	0.72	98.93	55%	5.8%	38%
2	99.3	>99.8	5.5	89.6	0.60	99.40	52%	5.9%	41%
Second Crop		99.6	6.1	45.0	3.89	89.93	21%	4.3%	13%
3	99.2	99.7	7.1	85.3	0.40	99.29	55%	7.5%	34%
4	98.6	99.8	3.9	91.8	0.10	99.90	47%	3.1%	40%
Second Crop		98.8	6.1	82.5	3.22	89.65	33%	nd	nd
5	99.7	99.7	8.0	83.2	0.64	99.18	59%	nd	nd

nd – Not Determined

Figure 16

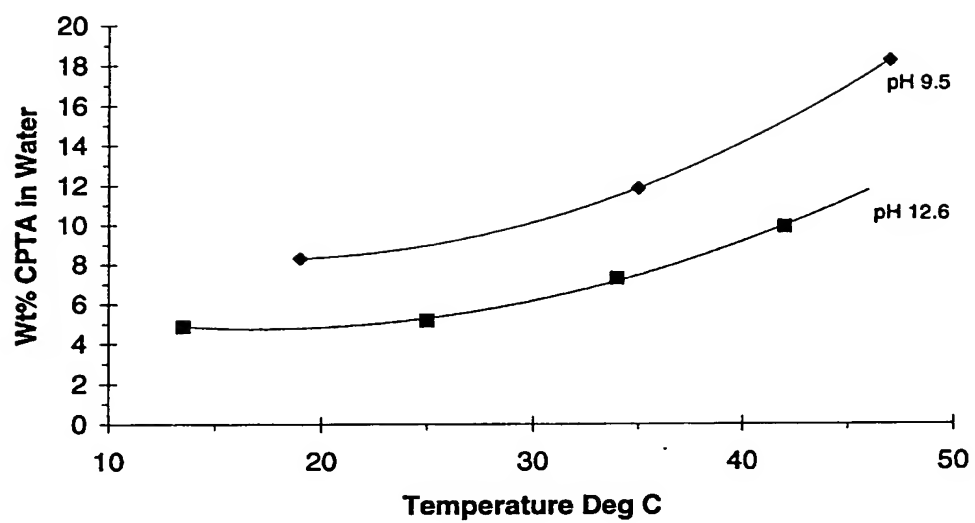


Figure 17

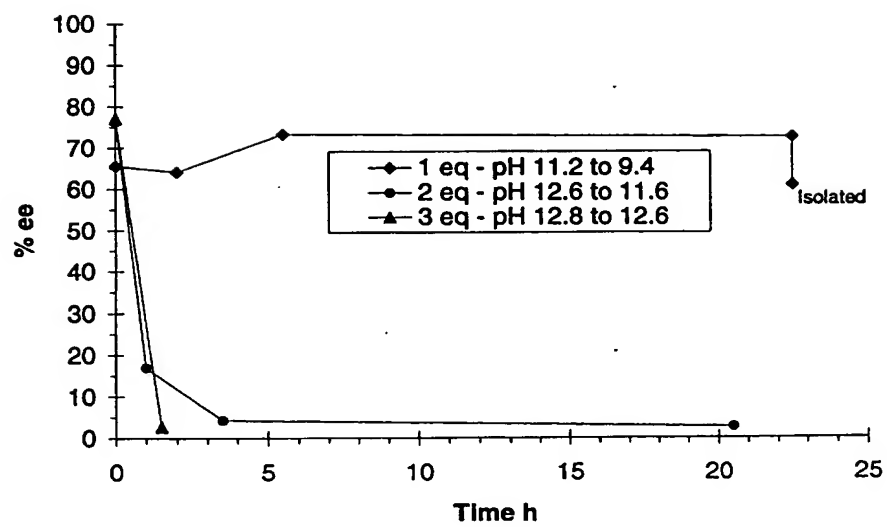


Figure 18

Recovered From:	Wt% Aqueous Sln	pH	mp °C	Recovery (+)/(-) Ratio	
Diastereomeric Salt	20.4	12.4	157.2-158.0	97%	0.1/99.9
“	20.1	12.1	160.4-161.0	98%	
“	19.6	nd	164.0-164.6	92%	
“	11.9	13.2	161.8-162.6	94%	
“	4.1	12	164.0-164.6	88%	0.1/99.9
Resolution ML	13.9	13	159.2-159.6	62%	
“	11.0	12.3	162.4-163.0	87%	
Combined ML & Salt	19.9	13	162.6-163.4	85%	
	TCI Americas Lot# FHG01		165.6-166.4		0.1/99.9

Figure 19

Solvent	Temp °C	Sample weight g	Sample Volume mL	Wt% CPTA in Solution
1,2-Dichloroethane	41	0.1558	25.00	32.3
	35	0.1360	25.00	27.6
	25	0.1455	10.00	18.8
	20	0.0489	25.00	15.3
	20	0.0505	10.00	14.0
	16	0.3230	25.00	11.0
	2.1	0.1300	10.00	6.05
Heptane	56	0.4641	25.00	3.39
	45	0.3331	25.00	2.11
	35	0.3823	25.00	0.767
	25	0.6750	25.00	0.413
	20	0.1994	10.00	0.17
	2.1	0.6038	25.00	0.057

Figure 20

pH	Temp °C	Sample weight g	Sample Volume mL	Wt% CPTA in Solution
9.4	35	0.3036	25.00	11.86
9.7	47	0.1111	25.00	18.28
9.5	19	0.2290	25.00	8.33
12.7	13.5	0.2012	25.00	4.89
12.6	25	0.3538	25.00	5.18
12.5	34	0.2320	25.00	7.30
12.5	42	0.3055	25.00	9.91

Figure 21

Wt Loaded g		Reflux Time	pH	HPLC Area% (+) / (-)	% CPTA	
(+)-Halofenate	50% NaOH				Assay	Isolated
8.65	1.67 (1 eq)	0 h	11.2	71.9/15.1		
		2		78.3/17.2		
		5.5		80.6/12.4		
		22.5	9.4	84.1/13.4		
		Oil		80.3/19.6	92%	81%
6.94	2.68 (2 eq)	0	12.6	83.4/11.3		
		1		56.8/40.4		
		3.5		49.0/45.0		
		20.5	11.6	47.5/45.0		
		Oil		48.7/51.0	103%	94%
7.28	4.21 (3 eq)	0	12.8	80.4/10.5		
		1.5	12.6	49.6/47.0		
		Oil		47.3/52.5	102%	88%